

REMARKS

Claims 1-40 and 43 have been cancelled and claims 44-72 have been added. Claims 41, 42 and 44-72 are pending. Claims 41 and 42 are withdrawn from consideration.

No new matter has been added by way of the above amendments. For example, new claim 44 corresponds to original claim 1 in combination with original claims 3, 5 and 7, and new claims 45 to 48 correspond to original claims 6 and 8-10, respectively. The embodiment in which a water-absorbing material is a "salt" is deleted in new claims 44 to 48. New claim 49 corresponds to original claim 1 in combination with original claims 3, 11 and 13, and new claims 50 to 54 correspond to original claims 14 to 18, respectively. New claim 55 corresponds to original claim 1 in combination with original claims 3, 19 and 21, and new claims 56 to 60 correspond to original claims 22 to 26, respectively. New claims 64 to 66 correspond to original claim 27, but are limited to embodiments in which the experimental animals according to claims 44, 49 and 55 are used, respectively. New claims 67 to 69 correspond to original claim 38. New claim 70 corresponds to original claim 43, but is limited to an embodiment in which the experimental animal according to claim 44 is produced. New claims 61 to 63 are dependent from new claims 44, 49 and 55, respectively. It is defined in these claims that the experimental animal according to claim 44, 49 or 45 can be used as a dry eye

model. According to the definition of dry eye given on page 12, lines 4-7 of the present specification, the corneal epithelial damage is encompassed in the symptoms of dry eye. Also, an animal having the dry eye-like symptom is described as a dry eye model on page 18, lines 12 to 16 of the present specification. New claim 71 is directed to a method of producing the experimental animal according to new claim 49. Lastly, new claim 72 is directed to a method of producing the experimental animal according to new claim 55. Thus, no new matter has been added.

In view of the following remarks, Applicant respectfully requests that the Examiner withdraw all rejections and allow the currently pending claims.

**Objection to the Drawings**

At pages 3 and 4 of the outstanding Office Action the Examiner has indicated that corrected drawings must be submitted in response to this Office Action. Applicant is concurrently submitting corrected formal drawings for review by the Official Draftsperson. Accordingly, this objection is moot.

**Objection to the Abstract**

The Examiner has objected to the Abstract for the reasons recited at page 4 of the outstanding Office Action. Applicant respectfully traverses and submits that a new Abstract of the Disclosure has been provided. Accordingly, this objection is

moot. Reconsideration and withdrawal thereof are respectfully requested.

**Objection to the Claims**

The Examiner has objected to claims 9, 13 and 21 for the reasons recited at page 4 of the outstanding Office Action. Applicant traverses these objections.

First, the Examiner asserts that in claim 9, line 2, the plural saccharides should be singular. Applicants submit that this subject matter, for instance as recited in claim 47, is recited in the singular sense. Regardless, the water-absorbing material is "at least one" saccharide selected from the group recited in claim 47. This rejection is moot. Reconsideration and withdrawal thereof are requested.

Second, the Examiner asserts that in claims 13 and 22 the recitation of "mammalian" should be "mammal". Applicant has adopted the suggestion in the newly added claims. Accordingly, this rejection is moot. Reconsideration and withdrawal thereof are respectfully requested.

**Issues Under 35 U.S.C. §101**

The Examiner has rejected claims 1-4, 7-12, 15-20 and 23-26 under 35 U.S.C. §101 asserting that the claimed invention is directed to non-statutory subject matter. Applicant respectfully traverses. Applicant notes that the present claims do not

encompass experimental animals such as human beings. Rather, the present claims encompass non-human mammals and fowl. Accordingly, this rejection is moot. Reconsideration and withdrawal thereof are respectfully requested.

**Issues Under 35 U.S.C. §112, first paragraph**

The Examiner has rejected claims 2, 4, 12, 20 and 28 under 35 U.S.C. §112, first paragraph asserting that the claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to make and/or use the invention. In particular, the Examiner asserts that the embodiment of the invention encompassing the animal model "wherein the corneal epithelial damage is dry eye" is not enabled. Applicant traverses and submits that the embodiment in which "corneal epithelial damage is dry eye" is no longer recited in the claims. Accordingly, this rejection is moot. Reconsideration and withdrawal thereof are respectfully requested.

The Examiner has also rejected claims 1-4, 7-12, 15-20, 23-28, 31-40 and 43 under 35 U.S.C. §112, first paragraph asserting that the specification, while being enabling for a non-human animal model, does not reasonably provide enablement for all experimental animal models as claimed. Applicant respectfully traverses and submits that the experimental animal has been limited to "a non-human mammal and a fowl." Accordingly, this

rejection is moot. Reconsideration and withdrawal thereof are respectfully requested.

In view of the above, Applicant respectfully submits that the present claims define subject matter which fully satisfies the requirements of 35 U.S.C. §112, first paragraph. Accordingly, the Examiner is respectfully requested to withdraw these rejections.

**Issues Under 35 U.S.C. §112, second paragraph**

The Examiner has rejected claims 29-34 under 35 U.S.C. §112, second paragraph for the reasons recited at page 9 of the outstanding Office Action. In particular, the Examiner asserts that although claims 29-34 are dependent upon claim 27 and recite "the experimental animal" of claim 27, claim 27 is drawn to a method of screening or evaluating medicine. Applicant traverses and submits that this issue is no longer present in the newly amended set of claims. Reconsideration and withdrawal of this rejection are respectfully requested.

**Issues Under 35 U.S.C. §102(b)**

The Examiner has rejected claims 1, 3, 5-8, 10 and 43 under 35 U.S.C. §102(b) as being anticipated by Gilbard et al. Applicant respectfully traverses this rejection.

As pointed out by the Examiner, Gilbard discloses an experimental animal having corneal epithelial damage caused by contacting an ocular cornea with a water-absorbing material, said

contacting being with the whole area of the ocular cornea, said animal being a rabbit, and said water-absorbing material being a hypertonic salt solution comprising an alkali metal salt and an alkali earth metal salt. Gilbard also discloses a method of making such an experimental animal.

However, the present invention as defined in new claims 44 to 48 and 70 is clearly distinguishable from the invention of Gilbard in that water-absorbing materials other than metal salts are used. Also, new claims 49 to 69, 71 and 72 correspond to original claims which were not rejected under this item. Therefore, the inventions as defined in each of new claims 44-72 are distinguishable from the invention of Gilbard.

Accordingly, Applicant respectfully submits that no anticipated based upon Gilbard exists. Accordingly, the Examiner is respectfully requested to withdraw this rejection.

Issues Under 35 U.S.C. §103(a)

The Examiner has rejected claims 27, 29-32, 34 and 38-40 under 35 U.S.C. §103(a) as being obvious over Yerxa et al., USP 5,900,407 (hereinafter referred to as Yerxa '407) in view of Gilbard and Fujihara. Applicants respectfully traverse this rejection.

Applicant points out that claims 27, 29-32, 34 and 38-40 have been cancelled and substantially replaced with new claims 64-66. Applicant further points out that while these previous claims,

such as claim 27, are now encompassed by new claims 64-66, new claims 64-66 are limited to embodiments wherein the experimental animals according to claims 44, 49 and 55, respectively, are used.

Yerxa '407 discloses a method of evaluating a medicine comprising damaging the corneal epithelial, administering medicine to the damaged area and evaluating therapeutic effect of the medicine. As admitted by the Examiner, Yerxa '407 fails to suggest contacting the corneal with a water-absorbing material. The Examiner has utilized the disclosure of Gilbard to discuss contacting the ocular cornea of an experimental animal with a water-absorbing material. However, as indicated above, the present claims, for instance claim 44 and claim 64 which depends thereon is distinguished from Gilbard. For instance, Gilbard fails to suggest or disclose water-absorbing materials other than metal salts. The other secondary reference of Fujihara fails to cure any of these deficiencies. Accordingly, the Examiner has failed to present a valid *prima facie* case of obviousness. Reconsideration and withdrawal of the rejection are respectfully requested.

However, even if, *arguendo*, the Examiner has hypothetically presented a *prima facie* case of obviousness, Applicants respectfully submit that the unexpectedly superior effects of the present invention rebut any hypothetical *prima facie* case of obviousness. As outlined in the present specification, for instance at page 13, lines 8-22:

In the model animal of the present invention, the corneal epithelium is made dry by dehydration and shows the symptom of corneal abrasion. Without medical treatment etc., this symptom can not be recovered or improved even if the ocular surface is moistened with lacrimal fluid and lasts for a long period of time, for example, more than 10 hours or, in some cases, dozens of hours. This enables persons engaged in this art to evaluate the therapeutic effect of medicines.

Such characteristics of the invention are of significant importance in that the corneal surface of the known compulsive eyelid retraction model (three hour retraction) is simply kept dried without abrasion, the dry eye-like symptom of said animal recovers in about an hour owing to secretion of lacrimal fluid, and thus said known dry eye model has some difficulty in the use for pharmacological evaluation of compounds.

The present invention is also characteristic in that the animal model can be prepared within about 60 minutes, preferably 20 minutes, after the eyelid retraction, while the known method requires 3 hours or longer to generate the compulsive eyelid retraction model.

The references cited by the Examiner are completely silent as to these unexpected effects according to the present invention. That is, the present invention unexpectedly allows those skilled in the art to correctly evaluate the therapeutic effects of medicine, to prepare an animal model in a shortened time period of about 60 minutes (rather than 3 hours), and to prepare an animal model having a pre-selected size of corneal damage and thus evaluate the change in symptoms by changes in the size. These results are superior and unexpected in view of the cited art. Accordingly, any hypothetical *prima facie* case of obviousness is rebutted.

In summary, Applicants respectfully submit that the Examiner has failed to present a valid *prima facie* case of obviousness.

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However, even if the Examiner has hypothetically presented a *prima facie* case of obviousness, it is rebutted by the unexpectedly superior results outlined above. Accordingly, the Examiner is respectfully requested to withdraw all rejections and allow the currently pending claims.

Applicants have attached hereto a marked up version of the claims to show the changes made for the Examiner's convenience.

If the Examiner has any questions or comments, please contact Craig A. McRobbie, Registration No. 42,874 at the offices of Birch, Stewart, Kolasch & Birch, LLP.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under § 1.17; particularly, extension of time fees.

Respectfully submitted,

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Attachment: Version with Markings to Show Changes Made

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Claims 1-40 and 43 have been cancelled.

Claims 44-72 have been added.